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Advances in Prevention of Radiation Damage to Visceral and Solid Organs in Patients Requiring Radiation Therapy of the Trunk

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Background: As a part of multimodality therapy, many patients with tumors of the trunk receive radiation therapy. The major morbidity of this therapy is often secondary to incidental radiation damage to tissues adjacent to treatment areas.
Methods: We detail our use of saline breast implants placed in polyglycolic acid mesh sheets to displace visceral and solid organs away from the radiation field.
Results: Analysis of CT scans and dose volume histograms reveal that this technique successfully displaces uninvolved organs away from the radiation fields, thereby minimizing the radiation dose to such organs and tissues.
Conclusion: We believe this is a safe and efficacious method to prevent radiation damage to visceral and solid organs adjacent to trunk tumor sites.
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KEY WORDS: radiation enteritis; saline breast implant; sarcoma; brachytherapy

INTRODUCTION

Multidisciplinary treatment of soft tissue sarcomas and other malignancies often includes adjuvant or neoadjuvant radiation therapy with wide resection and soft tissue reconstruction [1,2]. Radiation therapy has assumed an increasingly prominent role in the adjuvant treatment of many malignancies. Multimodality therapeutic plans including adjuvant or neoadjuvant radiation therapy are designed to treat primary tumor sites, areas at high risk for microscopic tumor extensions and/or regional lymph nodes thought to be at risk. Treatment plans are formulated with the intent of decreasing local recurrences and improving the potential for a cure while minimizing morbidity [3]. Organs with mucosal lining may develop a radiation mucositis during the course of treatment, the late effect often being formation of scar tissue [4]. The gastrointestinal tract, bladder, kidneys, liver, spleen, and lungs are particularly sensitive to radiation damage. The intestine is highly sensitive to radiation injury and is one of the most common organs limiting the dose of radiation that can safely be delivered to the abdominal wall, retroperitoneum and pelvis [5].

Multiple strategies have been developed to minimize radiation side effects. Strategies for minimizing radiation doses to critical organs can be divided into two main groups: (1) pharmacological manipulation to increase

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tolerance and therefore decrease radiation toxicity [6,7], and (2) mechanical strategies to avoid radiation exposure to sensitive organs [8–12].

Pharmacological manipulations demonstrated to be of possible efficacy in prevention of radiation enteritis include lumenal alkalinization resulting in neutralization of bile salts and pancreatic enzymes. Administration of nonsteroidal anti-inflammatory agents, methylprednisolone selected antioxidants, and lumenal administration of Lazaroid® have all been observed to afford mucosal protection [6]. Other investigators have demonstrated that significant prophylaxis against radiation injury to the bowel can be afforded by the feeding of an elemental diet for 3 days prior to and during radiation therapy [7]. Although of theoretical importance, none of these modalities have been shown to have sufficient efficacy to become a routine part of the radiation oncologist's armamentarium.

Clearly, the most efficacious method for preventing radiation damage to organs not requiring treatment is to exclude nontarget tissue from radiation exposure [5]. Whereas improvements in radiation dose delivery, especially customized Cerrobend™ (Arconium Specialty Alloys, Providence, RI) blocking, CT, and 3D treatment planning [3], are quite effective, in some cases critical organs lie next to the involved site, therefore still remaining the planned treatment field. At times, these critical structures can be mechanically displaced, resulting in radiation fields that encompass the tissues at risk while excluding radiosensitive tissues, such as bowel. Methods include the use of omental slings [8], polyglycolic acid mesh slings [10–12], tissue expanders [14], or gel implants [15,16] to suspend or displace bowel from the radiation field, as well as high dose rate intraoperative therapy given while sensitive tissues are held out of the field with surgical packing or instruments. Appropriate preoperative radiation treatment planning and/or brachytherapy allows treating tissues at risk and significantly reduces the dose to previously adjacent, but uninvolved, organs [5].

Recently, we have incorporated the use of saline filled, silicone-shelled breast implants in our methods of organ-displacement, prior to radiation therapy. We present two illustrative cases, one in which the implant was placed in the retroperitoneum after resection of a primary retroperitoneal sarcoma (Fig. 1A–C) and one in which the implant was placed in the pelvis after resection of a radiation-induced soft tissue sarcoma of the suprapubic area. Figure 2A, B illustrate the utility of this technique. In both cases, the implant was secured in a pocket or sac, created from polyglycolic acid mesh. These implants were placed by the surgical team in collaboration with the radiation oncologist and appropriately inflated and manipulated to displace radiation-sensitive tissues not felt to be at risk for tumor (Figs. 1B, 2B).

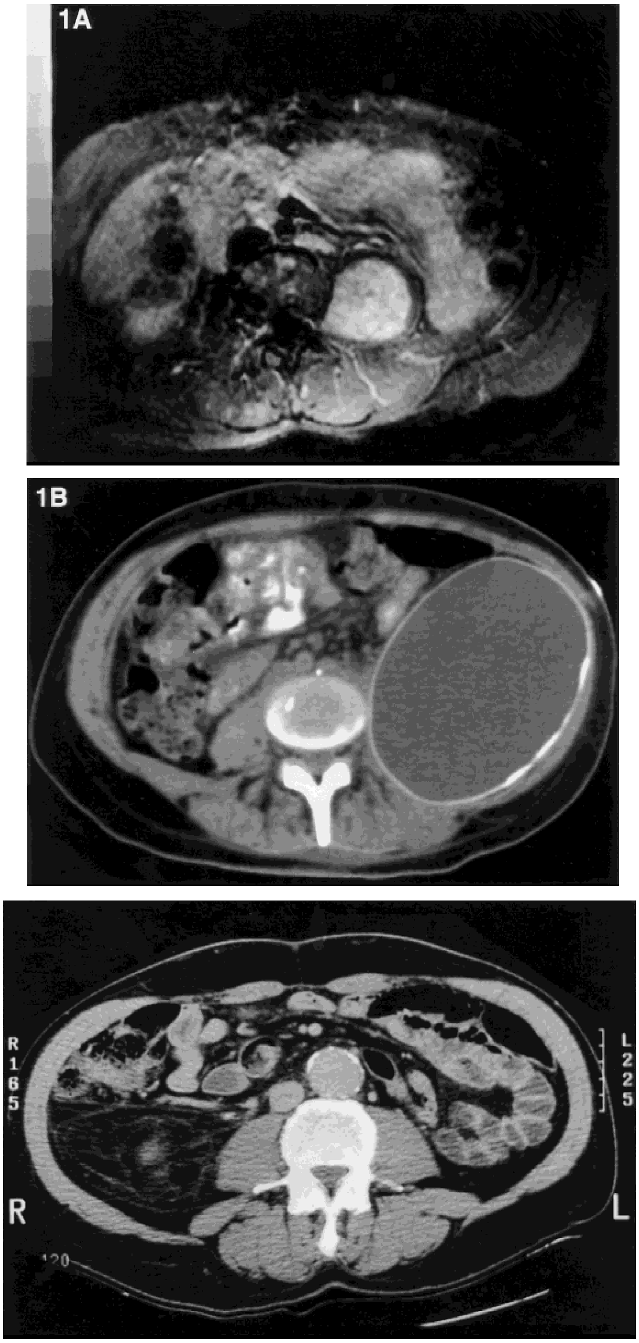

Fig. 1. **A.** Preoperative MRI scan showing close proximity of bowel and psoas tumor (patient 1). **B.** CT scan after tumor resection showing displacement of previously adjacent bowel by implants (patient 1).

SELECTION AND PLACEMENT OF TISSUE PROSTHESES

A sac was created by stapling or sewing polyglycolic acid mesh to the abdominal or thoracic wall. Then, the implant(s) was inserted into the pocket and filled with saline to the desired capacity. We have selected textured saline-filled, silicone-shelled breast implants due to their ready availability and their negligible dimension after

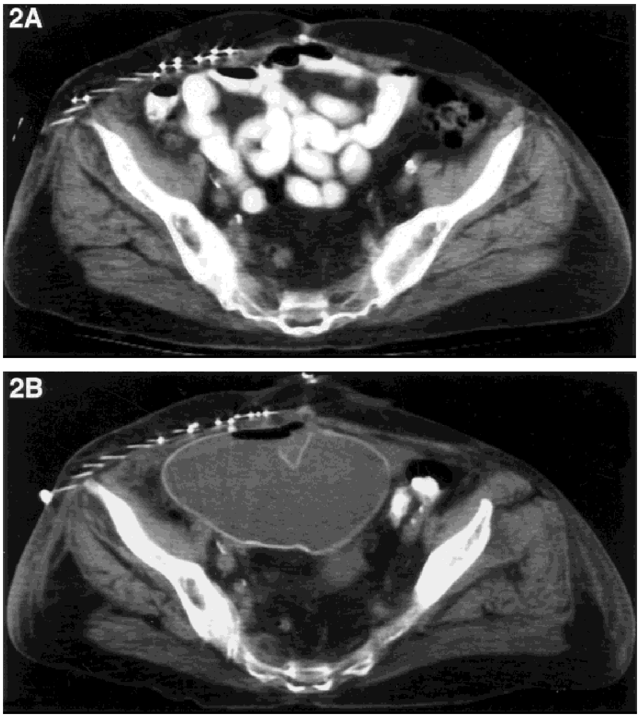

Fig. 2. **A.** CT Scan after resection of abdominal wall tumor showing close relationship of brachytherapy catheters (prior to loading) and previously irradiated bowel (patient 2). **B.** CT scan showing displacement of previously adjacent bowel and brachytherapy catheters by breast implant (patient 2).

deflation, which permits removal through a minimal incision using local anesthesia on an outpatient basis. We hypothesize that polyglycolic acid mesh controls the breast implant's position, decreases its interaction with bowel, and permits removal without dissection of bowel, after the implant is no longer necessary. By using an absorbable mesh, we are able to remove the implant through a minimal incision (overlying the implant) while leaving the mesh in place to dissolve, thus avoiding the need to dissect the bowel away from the implant. This technique possibly will decrease the problem of iatrogenic damage resulting in entrocutaneous fistula formation, both a theoretical and practical problem that has been reported previously [8].

RADIATION PLANNING AND TREATMENT

At our institution, radiation therapy is delivered by either an external beam approach (via linear accelerators) or brachytherapy (radioactive isotope implants). Surgical resection of the tumor is undertaken and followed by placement of saline-filled breast implants for organ displacement and placement of brachytherapy afterloading catheters when indicated. CT-based treatment planning is undertaken on a dedicated scanner and individualized treatment plans are formulated, often on the virtual (3-D) simulator [17]. Cerrobend™-blocked beams are precisely planned to limit dose to sensitive organs while delivering the necessary radiation dose to sterilize tumor in areas felt to be at high risk. We have been pleased with our ability to displace bowel from the areas at risk with minimal patient morbidity.

After placement of tissue expanders and intraoperative confirmation of appropriate placement by the radiation oncologist, patients undergo CT scanning with oral contrast (gastrografin) (Bracco Diagnostics, Morrow, GA). If brachytherapy was part of the treatment plan, orthogonal radiographs are taken to verify catheter position such that radiation dosimetry can be planned.

Studies have demonstrated that overlying tissue flaps have the potential to survive such therapy [18]. At a minimum of 5 days after surgery, the brachytherapy catheters are loaded with Iridium-192. If catheters are loaded sooner than this, wound complications increase in frequency [2].

Brachytherapy can be particularly useful in the treatment of disease that occurs in an area that has been previously irradiated. Placement of tissue implants as described herein can potentially increase the therapeutic index of such treatment [19], by decreasing exposure of radiation sensitive tissues, such as the small bowel, while delivering a high dose of radiation to the tumor or tumor bed that decreases very rapidly away from the plane of the implant.

The improved therapeutic index realized using an external beam approach is illustrated in Figure 3A,B. The dose volume histograms (DVH) illustrate the percentage of bowel that received at least the indicated dose. A Magnetic Resonance Image (MRI) obtained before the placement of the implant was utilized to determine the natural position of the bowel relative to the treatment fields.

ILLUSTRATIVE CASES

Case 1

A 39-year-old female developed a high grade malignant fibrous histiocytoma in her left psoas muscle with vertebral involvement. She required en bloc tumor and lateral vertebral process resection and bone grafting via a flank-retroperitoneal approach. During the initial procedure, after tumor resection, a 1,000 cc saline filled breast implant (R) was placed in the retroperitoneum and over expanded to 1,200 ccs. The wound was closed in layers. The patient received 6381 cGy to the tumor bed via external beam radiotherapy via a series of coplanar fields with multiple cone-downs planned on the 3D-virtual simulator. Fourteen days after cessation of radiation therapy, the patient underwent tissue implant removal through a 1 cm flank incision made through the old wound, under local anesthesia. A drain was placed and remained for 1 week. The patient's recovery was without complication. The patient did not experience signs or

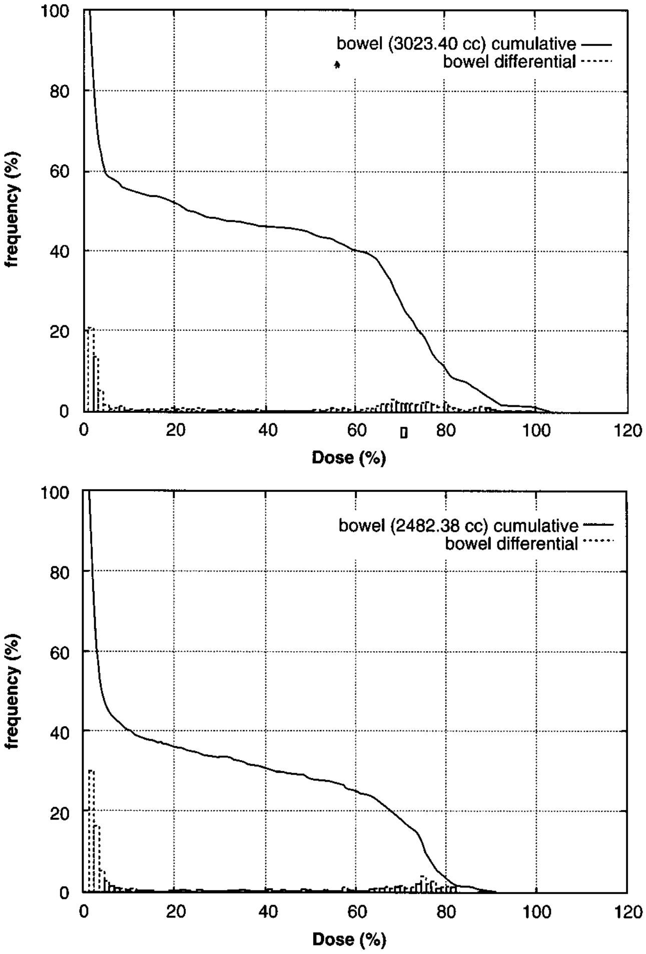

Fig. 3. **Top:** Dose volume histogram (DVH) showing cumulative (solid) and differential (dash) bowel doses (cGy) without saline-filled implant in place (patient 1). **Bottom:** DVH, which shows markedly decreased cumulative (solid) and differential (dash) bowel doses (cGy) with saline filled implant in place (patient 1).

symptoms of radiation enteritis. Her only significant complaint was of ''fullness'' in her abdomen, which resolved after prosthesis removal. The patient developed pulmonary metastases, but has no evidence of local recurrence.

Case 2

A 55-year-old patient developed a radiation-induced soft tissue sarcoma of the right lower abdominal wall/suprapubic area. Fifteen years prior to diagnosis, the patient underwent a total abdominal hysterectomy and bilateral oophorectomy for a mucinous cystadenocarcinoma of the left ovary and was treated with 4,000 cGy, utilizing rotational Cobalt 60 therapy. Complications from her original therapy included multiple bouts of radiation enteritis with bleeding over the years. The patient was explored at another institution for a right lower quadrant abdominal mass, which was initially thought to represent a hernia. It was at exploration found to represent a radiation-induced low grade liposarcoma and was incompletely excised. The patient was referred to our institution for further evaluation. She underwent wide re-excision and placement of brachytherapy catheters in the tumor bed followed by reconstruction using a contralateral rectus femoris flap. Histologic study revealed a low grade multifocal tumor with close margins of resection. During a second procedure, via a separate abdominal incision; a 1,000 cc implant was placed in the intraperitoneal space anterior to the bowel and bladder, in a pocket that was created out of vicryl mesh. After 5 days, the brachytherapy catheters were loaded and a dose of 4500 cGy at 1 cm was delivered over 5 days. The patient had a benign radiation therapy course. Five days after unloading, the saline-filled implant was removed without difficulty through a 1 cm McBurney incision.

CONCLUSION

The radiosensitivities of different cell types vary considerably. By mechanically displacing tissues not involved with tumor, out of the radiotherapy field, a significant therapeutic advantage can be achieved, leading to an enhanced radiobiologic effectiveness and minimization of long-term morbidity. In our experience with this technique, placement of silicon-shelled, saline-filled prostheses in a polyglycolic acid mesh pocket has proven to be an economical and efficacious modality. By creating an absorbable sac or pocket between the bowel and area at risk, the breast implant may stay in place for several weeks; no interaction between the bowel and breast implant occurs. The risk of bowel injury at the time of removal is therefore minimized.

We have described placement of saline-filled breast prostheses through an incision, as part of or as a sequel to an open surgical procedure, but we feel that minimally invasive techniques, involving the use of an endoscope and balloon dissector, may be suitable for placement in the case of patients who, for other reasons, do not require a large skin incision.

Placement of a silicone-shelled, saline-filled breast prosthesis in a polyglycolic acid mesh pocket has proven to be an economical and efficacious modality that can improve the therapeutic index of radiation therapy.

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COMMENTARY
Mechanical Displacement of Normal Tissue During Radiotherapy

Adjuvant radiotherapy of truncal sarcomas is fraught with potential toxicities. With the exception of breast lesions [1], the therapeutic ratio between disease control and damage to normal tissue is much narrower in the trunk than for similar lesions of the extremities. Consider the following table of tolerance doses for various vital organs [2] (Table I).

For microscopic epithelial cancers, a dose of 45–50 Gy will control 90% of subclinical disease [3]. Such a threshold has not been completely described for sarcomas, but appears to require a dose of >60 Gy [4]. This clearly increases potential risk of adjuvant radiotherapy of truncal sarcomas, even with today's sophisticated 3-dimensional treatment planning systems.

The technique described by Ritter and associates in the issue of the *Journal of Surgical Oncology* is an attractive way of using mechanical means to remove such potentially dose-limiting normal tissue from the radiotherapy portals. The authors rightly note that intraoperative radiotherapy may allow the same effect; the single randomized trial of that modality in retroperitoneal sarcomas has yielded a local control advantage over control therapy, without survival benefit [5].

Frequently, however, the answer is much simpler; consider the case in Figure 1. This 64-year-old man presented with a large right retroperitoneal sarcoma. As shown, the lesion itself provided a significant amount of mechanical displacement. Preoperative radiotherapy of 50 Gy would require far less normal tissue to be treated than postoperatively, when the same radiotherapy portals would include bowel which had returned to its normal position after removal of the lesion. Preoperative radiotherapy additionally takes advantage of maximal oxygenation of the lesion and potentially decreases the likelihood of tumor seeding at time of surgery. The postoperative radiotherapy boost under these circumstances would then simply entail a smaller tumor bed dose delivered via brachytherapy or conventionally fractionated radiotherapy. Use of the Duke technique described above would dovetail nicely under these circumstances, and would further decrease the dose to dose-limiting normal tissues.

TABLE I. Defined as the TD5/5, or the Dose at Which 5% of the Population Would Develop the Toxicity at 5 Years.

Organ	Toxicity	Dose (Gy)
Lung	Pneumonitis	17.5
Kidney	Nephritis	23
Liver	Hepatopathy	30
Small Bowel	Obstruction	40

We must not underestimate the importance of such mechanical innovations in clinical radiotherapy. In surgery of rectal cancer, operative interventions to keep small bowel from the pelvis for subsequent radiotherapy are routine, and contribute to higher tolerable doses. Absent any likely advances soon in chemotherapy or radiosensitization of sarcomas, it is good to be reminded that the therapeutic ratio may be enhanced by simple measures—potentially even by when we perform the adjuvant radiotherapy.

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